REMARKS

The abstract of the disclosure is enclosed on a separate sheet in accordance with 37 CFR 1.52(b)(4) is a copy of a replacement abstract regarding Application No. 10/523,761.

Claims 5 and 6 now stand objected to under 37 CFR 1.75(c) as allegedly being in improper form because a multiple dependent claim should refer to other claims in the alternative and/or cannot depend from any other multiple dependent claims. Applicant has reviewed the Examiner's objections and has revised claims 5 and 6 where appropriate. Full reconsideration is respectfully requested.

Claims 1-4 now stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Krishnamurthy et al. (US 6,419,960). Krishnamurthy et al. allegedly teaches an oral modified/controlled release drug formulation that provides rapid initial onset effect and a prolonged duration of effect. The claims were amended for further clarification. Full reconsideration is respectfully requested.

Claims 1-4 now stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Devane et al. (US 6,228,398). Devane et al. allegedly teaches a multiparticulate modified release composition that delivers an active ingredient in a bimodal manner. The claims were amended to address the concerns identified in the report. Full reconsideration is respectfully requested.

Before commencing any rebuttal with reference to any alleged prior art issues the Examiner is respectfully directed towards the following excerpted case law from which Applicant will draw liberally. The following excerpts of U.S. case law represent Applicant's understanding of the test for novelty and obviousness.

ANTICIPATION

In Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986) ("It is axiomatic that for prior art to anticipate under § 102 it has to meet every element of the claimed invention, and that such a determination is one of fact.").

In re Donohue, 766 F.2d 531, 226 U.S.P.Q. 619, 621 (Fed. Cir. 1985) ("an anticipation rejection requires a showing that each limitation of a claim must be found in a single reference, practice, or device.").

In Atlas Powder Co. v. E.I. du Pont De Nemours & Co., 750 F.2d 1569, 1574, 224 U.S.P.Q. 209, 411 (Fed. Cir. 1984) ("exclusion of a claimed element from a prior art reference is enough to negate anticipation by that reference").

In Tights, Inc. v. Acme-McCrary Corp., 541, F.2d 1047, 191 U.S.P.Q. 305 (4th Cir. 1976); Saf-Gard Prods., Inc. v. Service Parts, Inc., 532 F.2d 1266, 190 U.S.P.Q. 455 (9th Cir. 1976); Shanklin Corp. v. Springfield Photo Mount Co., 521 F.2d 609, 187 U.S.P.Q. 129 (1st Cir. 1975) ("To anticipate under section 102, a prior art reference must disclose all the elements of the claimed invention or their equivalents functioning in essentially the same way.").

In re Beno (1985) 768 F.2d 1340, 226 U.S.P.Q. 683 (Fed. Cir. 1985) a prior art patent or published application is a reference only for that which it teaches.

Simply stated, a prior publication or patent description will be considered as anticipatory when its disclosure is at once specific and enabling with regard to the particular subject matter at issue. . . .However, such disclosure may yet be held not to legally anticipate the claimed subject matter if it is found not to be sufficiently enabling, in other words, if it does not place the subject matter of the claims within "the possession of the public".

Based on the Examiner's rejection of the claims, Applicant has made amendments that clearly distinguish the invention from the cited art. Applicant has amended previous claims 1-6 and submits amended claims 1, 3-5, (and newly presented claims) 7-11 for further consideration.

Referring now to the Examiner's 35 U.S.C. 102 (b) rejection with respect to Krishnamurthy et al. U.S. Patent 6,419,960 hereinafter referred to as the '960 Patent, there is taught a complex process for preparation of a modified / controlled release oral drug formulation. This process comprising the following essential steps:

1) Preparation of immediate release beads by coating of the core sugar beads as disclosed in Example 1.

2) Preparation of controlled release beads by coating of the immediate release beads of step 1 with polymer coating as described in Example 2.

3) Enteric coating of controlled release beads as described in Example 3 of step 2.

4) Apply an immediate release coating on the enteric coated controlled release beads as described in Example 6.

This process requires at least three top coating procedures taking place in the Aeromatic Fluid Dry Bed, and at least two different enteric coating polymers, on the sugar core beads. A number of additional components are required in order to prepare controlled released multilayer beads. Respectfully, the teachings of the '960 Patent therefore are quite complex in relation to Applicant's invention. The composition of Applicant contains only two compounds: the active ingredient and the polymer, which are compressed, then ground and screened. There is no use for sugar beads and there is no need to coat the granules prior to filling into the capsules. Therefore Applicant's composition of modified release granules is in many ways superior to the prior art, and preparation is much simpler and therefore preferable.

Applicant submits that the present application discloses and claims a composition which contains only two components: the drug and the polymer. The particles of the composition are not coated. The ratio of the polymer to the drug is between 4 and 100 while none of these limitations appears in the '960 Patent. The multilayer beads of the '960 Patent contain sugar, talc, triethyl citrate, film forming agent methylphenidate and polymers. Further the particles of the '960 Patent are coated four times and the ratio of the polymer to drug is about one. Clearly the '960 Patent does not meet every element of Applicant's claimed invention and therefore cannot anticipate the amended set of claims, pursuant to accepted jurisprudence set out above, for example In Re: Donohue.

In addition Applicant respectfully submits the Examiner has erred in the calculation of the weight ratio of the enteric polymer to the drug. An explanation follows below.

Examples 1, 2, 3 and 6 of the '960 Patent describe the process of preparation of the multilayered beads by applying additional coatings on top of the previously prepared beads. Therefore the beads in example 6 which represents 91.4% of the composition are actually beads from example 1 after three coating applications. One particularly important fact is that the main composition of the beads in example 1 is sugar which represents 80% of the composition. Consequently sugar constitutes about 53% of the final multilayer beads.

Accordingly the final multilayered beads contain about 16% of methylphenidate and about 16% of the polymer Eudragit®. Therefore the ratio of polymer to drug is about 1 and not about 14 as was incorrectly asserted by the Examiner. The supporting calculations were made by simple mathematical extrapolation and can be submitted upon request.

Therefore Applicant submits that the '960 Patent does not teach a ratio of enteric polymer to drug of greater than 4 and less than 100. It further does not teach a composition for oral administration which achieves drug release in two spikes, yet which comprises uncoated particles since the '960 Patent teaches beads which are enteric coated more then once. The composition of the '960 Patent does not consist essentially of drug and polymer, but includes more then 50% of sugar. Applicant further states that the '960 Patent does not disclose all of the elements of the claimed invention or their equivalents functioning in essentially the same way. Reconsideration is respectfully requested.

Out of an abundance of caution Applicant also submits that the present claim set cannot be obvious to one skilled in the art with respect to the '960 Patent following the tenants of Graham v. John Deere for the same reasons set out below.

OBVIOUSNESS

The traditional test enunciated in Graham vs. John Deere Company 383 U.S. 1, 148 U.S.P.Q. 459 1966, for Section 103 non-obviousness requires the fact finder to make several determinations. The test provides that the scope and content of the prior art be determined, the differences between the prior art and the claims at issue be ascertained, and the level of ordinary skill in the pertinent art be resolved. Thus, the patentability of the claims at hand must stem from the fact that the specific combination of the claimed elements was not disclosed in the prior art and the additional allegation that the specific combination of claimed elements was non-obvious to one of ordinary skills in the art.

Clearly, the prior art does not suggest or provide any reason or motivation to produce the composition for oral administration which achieves drug release in two spikes, while the composition comprises a single population of uncoated particles of a homogenous mixture consisting essentially of methylphenidate or a salt thereof and an enteric polymer, wherein the ratio of enteric polymer to drug is greater then 4 and less then 100.

In order to provide a "dual spike" delivery and providing an immediate spike that provides a rapid elevation of the concentration of the drug in the blood, a substantial amount of drug should be dissolved as soon as possible. But in order to provide delayed release as well, the dissolution of a substantial amount of the drug should be prevented from ingestion in the stomach by insulation of the drug from the acidic medium of the stomach. The enteric polymer in Applicant's case serves the function of the insulation. As presented in the disclosure on p. 3, lines 2-11, the increase of the particle size and the ratio of enteric polymer to drug provides the dual spike drug outcome.

An increase of particle size is contrary to the teachings of the prior art and the knowledge of the person skilled in the art since the art points towards a reduction of particle size in order to facilitate drug dissolution by increasing the available surface area. Applicant has discovered that in Applicant's particles of a larger size only the drug content that is closest to the surface of each particle leaches from the mixture and dissolves in the acidic gastric fluid of the stomach. Dissolution of the drug is reduced for the portion of the drug that is located deeper in the particles which is protected against dissolution by the remaining enteric polymer. Further dissolution is delayed until the particles reach the small intestine where the pH is high enough so that the enteric polymer dissolves to release the balance of the drug. By varying the polymer/drug ratio and hence increasing the size of Applicant's granules one can control the percentage of the drug released in each spike. Finally Applicant's invention teaches increasing particle size and also eliminates the requirement for surface coatings and for a seed core. Hence Applicant's invention is unexpected and contrary to the direction pursued in the prior art represented by the '398 Patent and the '960 Patent.

Referring now to the Examiner's 35 U.S.C. 103 rejection with respect to Devane et al. U.S. Patent 6,228,398, hereinafter referred as the '398 Patent, the Examiner states that the '398 Patent teaches a modified release composition containing methylphenidate, as well as coating of modified release solution with polyvinyl pyrrolidone. Polyvinyl acetate phthalate is also taught as a coating material. However there are some substantial differences between the teachings of the prior art and Applicants claim set.

The '398 Patent describes the two spike release or the delivery of a population of two types of beads. This represents a simple combination of immediate release granules along with delayed release granules with the combination of those two populations being in one capsule. Applicant's composition however contains only one single population of granules which are

capable of delivering the drug in two spikes. Therefore the teachings of the current claims require only one type of granule comprising the active ingredient and polymer prepared and filled into capsules without any surface coating beforehand. According to the teachings of the '398 Patent there is a requirement to produce two separate populations of granules. The first is an immediate release component prepared by surface coating of the nonpareil seeds in the fluid bed coating apparatus. A second batch of modified release beads is prepared by surface coating of the immediate release components with polymer in the fluid bed apparatus. Following the preparation of two separate batches the capsules are to be filled with two populations of different granules.

Therefore the '398 Patent differs from the amended claims since it teaches surface coated granules in the composition whereas Applicant has uncoated granules. The '398 Patent teaches two types of granules in the composition whereas Applicant has only one type of granule. The granules in the '398 Patent require a core seed whereas Applicant has no core. The polymer/drug ratio in the '398 Patent is also out of limits of the ratio claimed by Applicant.

As it apparent from the prior art, various techniques for preparation of medication with modified drug release is known. However most of those techniques required some type of surface coating of the particles in order to prevent immediate release of the drug. There is no prior art teaching of achieving delayed release without surface coating in the manner provided by Applicant.

There is no motivation from the '398 or '960 Patents to produce a single population of particles which result in dual release without surface coating as taught in the Applicant's amended claims. The teaching of the '398 Patent is a combination of different particles with different characteristics. There is a lack in the art or motivation to one skilled in the art of providing one type of particle which achieves dual release. The use of a single population type of uncoated particles in a composition for oral administration which achieves drug release in two spikes was not suggested or taught directly or indirectly in the prior art and therefore the claims as amended cannot be rendered obvious to the person skilled in the art because of either of the '960 or the '398 Patents.

The prior art teaches use of small particles used to increase dissolution of the components by increasing the total surface area of the particles. On the contrary Applicant increases the size of the granules beyond a #16 mesh screen and thus provides the unique features heretofore

unknown. Particularly the preferred granules claimed by Applicant are in the range of falling between a #16 and a #8 mesh screen and therefore the size of the particles or their effective diameter would be in the range between 1.58 mm and 3.17 mm. The particles used in the '398 Patent, as illustrated in example 1 (col. 12), have the diameter range between 0.5 mm-0.85 mm. Assuming that after coating their volume increases two fold, their diameter would increase to 0.63-1.071 mm which is still smaller than mesh size #16 being 1.58 mm. The calculations were performed using simple math and can be provided upon request. There is no teaching in the prior art in the direction of increasing particle size beyond the #16 screen size yet providing dual spike activity and therefore the cited prior art cannot render obvious the present claim set to one person skilled in the art.

Finally most of the teaching in the prior art relates to surface coating particularly using core granules or seeds which are further coated with the active ingredient and additional top coatings. Therefore those granules or seeds which are made of sugar or another non-therapeutic ingredient, represents the essential weight of the compounds. The main ingredient in Applicant's composition is the enteric polymer. There is no teaching or motivation in the cited prior art to eliminate the core seeds from the formulation. There is no teachings in the prior art suggesting that the ratio of polymer to the drug should be in the range of 4 to 100. The '398 Patent teaches the ratio of polymer to drug of about 2:1 in a modified release component and 0.3:1 in the immediate release component which is less then 4. The '398 Patent does not suggest an increase in the ratio of polymer to drug to the range of 4 to 100. Therefore the ratio claimed by Applicant was not obvious to the person skilled in the art, but is an important element of the invention.

Applicant submits that the present claim set teaches an improved composition which achieves drug release in two spikes while comprising only a single population of uncoated particles of a homogenous mixture consisting essentially of a drug and an enteric polymer. The ratio of enteric polymer to the drug is greater then 4 and less then 100. The combination of properties for obtaining the required result namely the drug released in two spikes was not taught nor suggested in the '398 Patent or the '960 Patent and one skilled in the art was not motivated from the prior art to arrive at Applicant's claims as amended.

Applicant, according to the Patent Office Practice of considering obviousness as set out in Graham vs. John Deere, has assessed the prior art, specifically the '398 Patent and the '960

Patent and has arrived at the conclusion that nothing within the teachings of the '398 or ,960 Patents would result in the composition taught in Applicant's amended claim set.

In Conclusion, Applicant has addressed all the issues raised in the Examiner's Report of November 7, 2007 and respectfully requests full reconsideration of all rejections for the reasons set out above.

In view of the above submissions, Applicant respectfully submits that this application is now in condition for allowance and the same is solicited at the Examiner's earliest convenience.

If the Examiner has any questions, he is requested to contact Evgeny Amelchenkov at (905) 771-6414.

Respectfully submitted,

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NHH/EA/lvp
Encl. Amended Abstract
Petition For Extension of Time